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$SnCl_2/PdCl_2$-mediated aldehyde allylation in fully aqueous media

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Abstract—Catalyzed by $PdCl_2$, $SnCl_2$ can efficiently mediate the allylation of various aldehydes with allyl chloride or bromide, but not with allyl alcohol, in fully aqueous media. The yield of the reaction is very high (90–100%), and the reaction is operationally simple, environmental benign and easy to scale up.

Carbonyl allylation is a useful approach to the homoallylic alcohols product, which is a versatile subunit that can easily be converted to a number of other useful functions.[1] To achieve carbonyl allylation, traditionally one needs to prepare a certain allylic organometallic reagent at first and then add it to the carbonyl compound in anhydrous organic solvents. Because the allylic organometallic reagent is unstable towards air and moisture, this synthesis approach is neither operationally simple nor safe to scale up.

An alternative approach to achieve allylation has been developed by Masuyama and co-workers.[2,3] In this approach, allylic alcohol directly reacts with the carbonyl compound yielding the homoallylic alcohol in one pot via an umpolung of π-palladium complexes. $SnCl_2$ is used as a reducing reagent and various Pd^{2+} complexes are used as catalyst. Many organic solvents such as DMF and THF can be used as the solvent. The yields are usually 50–80%.[4–6]

Our recent interest in the organic reactions in aqueous media[7] prompted us to study whether we can perform Masuyama allylation reaction in fully aqueous media. We believe that such a fully aqueous version of Masuyama reaction may bring about significant improvements over the original procedure due to the following reasons. (1) Fully aqueous allylation is much cheaper and simpler to operate. (2) Fully aqueous allylation is very safe and environmentally benign. Therefore, it is ideal for large-scale industrial and laboratorial synthesis.

Our initial attempt to accomplish the fully aqueous $SnCl_2$/Pd(II)-mediated allylation with allylic alcohols was not successful. In agreement with Masuyama's work[2] we found that the allylation reaction is not severely quenched by the presence of a little water. However, the reaction yields decrease dramatically when a large amount of water is added to the reaction mixture (see Table 1). In the fully aqueous solution, the allylation yield is only 29.5%.

Despite the low yields associated with allyl alcohol, we found that with allyl chloride or bromide we could obtain very high yields of the homoallylic alcohol products using the $SnCl_2/PdCl_2$ in fully aqueous solution. For example, the reaction between allyl chloride and benzaldehyde in H_2O over 16 h at room temperature provides the allylation product almost quantitatively. Similar results can also be achieved using THF or 1:1 THF/H_2O media. Therefore, the addition of water does not significantly affect the yield of this $SnCl_2/PdCl_2$-mediated allylation reaction with allyl chloride.

On the basis of the above findings, we developed the $SnCl_2/PdCl_2$-mediated allylation reaction to a practical synthetic methodology (Scheme 1). We found that $PdCl_2$ is sufficient for the reaction. Compared to the previous studies, this ligand-free catalysis is much less resource demanding. A variety of carbonyl compounds were tested. The experimental results are summarized in Table 2.

Keywords: Allylation; $SnCl_2$; Palladium; Aqueous medium.

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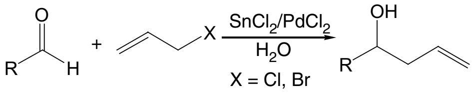
Table 1. Effect of water on the $SnCl_2/PdCl_2$-mediated allylation of benzaldehyde[a]

Entry	Substrate	Solvent	Yield (%)
1	Allyl alcohol	THF	>99
2	Allyl alcohol	THF/H_2O (4:1)	95.0
3	Allyl alcohol	THF/H_2O (3:2)	62.0
4	Allyl alcohol	THF/H_2O (2:3)	58.8
5	Allyl alcohol	THF/H_2O (1:4)	44.8
6	Allyl alcohol	H_2O	29.5
7	Allyl chloride	THF	>99
8	Allyl chloride	THF/H_2O (1:1)	>99
9	Allyl chloride	H_2O	>99

[a] All the reactions were performed for 16 h at room temperature. The concentrations of all the reactants are the same for all the reactions. The yields were determined using ^1H NMR.



Scheme 1.

According to Table 2, both allyl chloride and bromide can be used, although allyl bromide usually provides a higher yield. Most of the allylation reactions provide 90–100% yields. These yields are higher than those achieved using Masuyama's procedure.

However, the attempt to allylate aliphatic ketones (entry 17) fails, whereas aromatic ketones (entry 18) may only be partially allylated with more reactive allyl bromide. Both aromatic or aliphatic aldehydes can be well allylated. For, β-unsaturated aldehydes (entry 5), allylation only provides the 1,2-addition product. Furthermore, when cinnamyl halides (entries 15 and 16) were used, the

Table 2. Carbonyl allylation mediated by $PdCl_2/SnCl_2$ in water using allyl chloride or bromide[8,9]

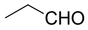
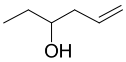
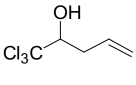
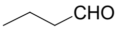
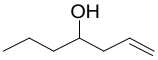
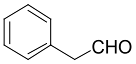
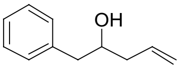
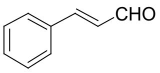
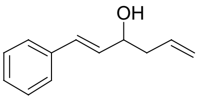
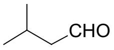
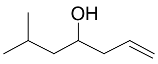
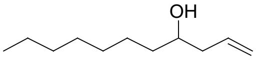
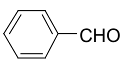
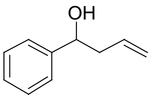
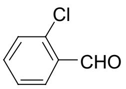
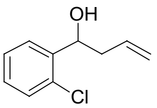
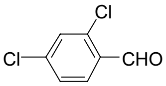
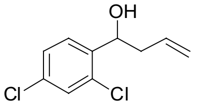
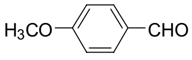
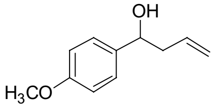
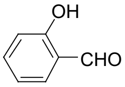
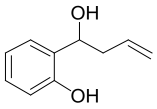
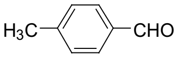
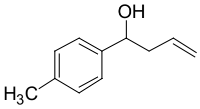
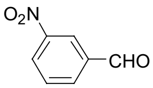
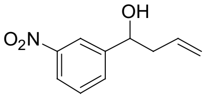
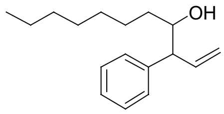
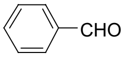
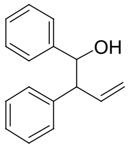
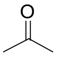
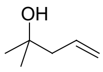
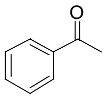
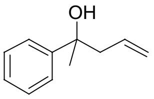
Entry	Substrate	Product	X	Yield (%)[a]/time (h)
1			Cl Br	92/16 93/16
2	CCl_3CHO		Cl Br	88/16 93/16
3			Cl Br	91/16 93/16
4			Cl Br	92/16 95/16
5			Cl Br	95/16 98/16
6			Cl Br	94/16 96/16
7	$CH_3(CH_2)_6CHO$		Cl Br	>99/16 >99/16
8			Cl Br	>99/16 >99/16
9			Cl Br	>99/16 >99/16

Table 2 (*continued*)

Entry	Substrate	Product	X	Yield (%)[a]/time (h)
10			Cl Br	>99/16 >99/16
11			Cl Br	95/16 97/16
12			Cl Br	>99/16 >99/16
13			Cl Br	>99/16 >99/16
14			Cl Br	51/18 93/24
15[b]	$CH_3(CH_2)_6CHO$		Cl Br	87/16 (83:17)[c] 98/16 (85:15)
16[b]			Cl Br	71/16 (62:38) 83/16 (91:9)
17			Cl Br	Trace/24 Trace/24
18			Cl Br	Trace/24 68/72

[a] Based upon ^{1}H NMR analyses of the products, except for entries 1, 2, 3 and 6 whose yields were calculated using the weights (i.e., isolation yields).

[b] Reaction between aldehydes and cinnamyl halides.

[c] Diastereoselectivity (*anti*:*syn*).

allylation reaction exhibits very high regio-selectivity as only the α-addition products are obtained. The reaction is also modestly diastereoselective as more *anti* products are observed (entries 15 and 16).

It is noteworthy that recently a number of zero-valent metals have also been found to be able to mediate the carbonyl allylation reaction in water.[10,11] However, because zero-valent metals are not soluble in water, it is difficult to scale up these reactions for large-scale synthesis. Irregular reactivity of the zero-valence metals due to the surface metal-oxide is also a problem frequently encountered in these reactions. Compared with these reactions, $SnCl_2$ and $PdCl_2$ used in the present procedure are both very soluble in water. Therefore, the present reaction is easy to scale up and highly reproducible. Little product can be obtained if soley $SnCl_2$ or $PdCl_2$ is used in the reaction. According to Masuyama's studies,[2,3] the $SnCl_2/PdCl_2$-mediated allylation may involve an η^3-allyl-Pd complex intermediate. Allylation of aldehydes possibly occurs with the in situ generated allyltin compound to afford the final products.

In summary, we have demonstrated that $SnCl_2/PdCl_2$ can efficiently mediate the allylation of various aldehydes with allyl chloride or bromide, but not with allyl alcohol, in fully aqueous media. The reaction is operationally simple and environmentally benign. It stands for a significantly improved procedure over Masuyama's $SnCl_2$/Pd(II)/allyl alcohol procedure where the yields are lower and highly polar aprotic organic solvents must be used.

Acknowledgements

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8. Typical procedures for the allylation are as follows: To a mixture of carbonyl compound (4 mmol) and allyl halide (8 mmol) in water (20 mL), $PdCl_2$ (0.2 mmol) and $SnCl_2$ (8 mmol) were added. The mixture was vigorously stirred at room temperature for several hours, before extracted with ether (3 × 30 mL). The combined organic layers were dried over anhydrous $MgSO_4$ and evaporated. The residue, in most cases, afforded the corresponding homoallylic alcohols with sufficient purity as judged by TLC and ^{1}H NMR without the need for further purification.
9. All the final products were characterized using ^{1}H NMR, ^{13}C NMR, IR and elemental analysis.
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